BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Application Number: 10/772,809
Filing Date: February 5, 2004
Appellant(s): Bernstein, Joel E.

Alice O. Martin
For Appellant

REPLY BRIEF

This is in response to the Examiner's Answer Mailed August 6, 2010 ("Answer").

Claims 9, 11, 12, 14, 15 and 17 are pending.

I. Crawford Does Not Anticipate Claims 9, 11, 14-15

The examiner discounts the argument against anticipation that Crawford's intended use differs from that of present claims. However, as discussed in the following table, dosages differ and this is an important difference based on intended use. Note that claim 17 is not included in the rejection - it includes specific dosages. The present claims are to a composition that provides increased pain relief. Crawford does not teach increased pain relief so there is no proof his composition is "structurally" the same as presently claimed. The cases cited by the examiner *In re Casey*, 152 USPQ 235 (CCPA 1967); *In re Ott*, 136 USPQ 458, 459 (CCPA 1963) did not involve pharmaceutical compositions, the present invention. The "manipulative difference" to which the examiner refers was to a "process of making," in the cases cited not a composition as herein. The cases related to hair curlers and an adhesive taping machine. No differences except intended use were given.

The examiner also discounts the argument that the Crawford composition includes more than the "consisting essentially of" limitation of present claim 9 (and dependent claims 11, 12, 14 and 15). Although it is true that examiners treat "consisting essentially of" as "comprising" for search purposes, this limitation in claim interpretation means other ingredients of Crawford, notably piroxicam, are not in the compositions presently claimed on appeal. The other Crawford ingredients make that composition structurally different from the present composition, therefore the different intended uses are relevant. The following table provides further explanation of this argument.

Publication	Comments	Relationship to U.S. Patent Application No. 10/772,809
Crawford	Crawford reports an "improved" anti-inflammatory composition including piroxicam or a salt of piroxicam and a "gastric antiirritation and ulcer-inhibiting amount of doxepin or a salt of doxepin". Crawford states that the doxepin is incorporated into the composition solely to reduce gastric irritation/ulceration from the piroxicam.	1. There is no teaching whatsoever in Crawford that combining a tricyclic antidepressant with a non-narcotic NSAID would provide a useful composition for treating pain. 2. Table I of Crawford shows that the gastric antiirritation/ulcer reducing potential of doxepin could be demonstrated for oral doses of from 3.3 to 33 mg/kg. Since the average body weight in 2002 (Exhibit C) of an

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		American woman was approximately 75 kg and an American man 87 kg, these doxepin dosages translate into 248 mg – 2480 mg as a single oral dose for women and 287 mg – 2870 mg as a single oral dose for men. This is versus ≤25 mg doxepin daily in 10/772,809. 3. It is important to note that while all NSAIDs are generally recognized as producing gastric irritation and potential ulceration, the only NSAID Crawford proposed be combined with doxepin is piroxicam. One should ask, why didn't Crawford teach or claim that doxepin could be utilized in combination with a variety of widely utilized NSAIDs that are gastric irritants, including naproxen, ibuprofen, ketoprofen, diclofenac and indomethacin? The answer is, "the risk for piroxicam might be higher than for the other NSAIDs" (Martindale The Complete Drug Reference, 35th Edition). It is generally recognized that the adverse gastrointestinal effects of NSAIDs are due to inhibition of cyclo-oxygenase-1 (COX-1) and that inhibition of COX-2 improves gastrointestinal tolerance. Piroxicam has selective COX-1 inhibitory activity which most likely accounts for its greater gastric irritating effects than the other widely utilized NSAIDs, which have a mixture of COX-1 and COX-2 inhibitory effects. This then is further confirmation that any teaching of Crawford regarding a composition is only for a composition of piroxicam and no suggestion, much less teaching, by Crawford that the piroxicam-doxepin combination would have any analgesic activity beyond that conveyed by the dose of piroxicam utilized.

II. The Combination of Crawford, Caruso and Matheson Does Not Make Claims 12 and 17 Obvious

Crawford is discussed in Section I herein. The examiner cites Caruso for providing doxepin in salt form, and Metheson for rofecoxib.

As shown in the enclosed table, those of skill in the art would not be led to combine Caruso and Matheson with Crawford.

Publication	Comments	Relationship to U.S. Patent Application No. 10/772,809
Caruso	Caruso relates neuropathic pain is pain that is due to functional abnormalities of the nervous system. There is a composition and method for alleviating neuropathic pain which comprises co-administering "at least one antidepressant in an amount sufficient to alleviate neuropathic pain and at least one non-toxic NMDA receptor antagonist." The therapeutic composition so described may contain "a therapeutically effective amount of at least one other pharmacologically active substance." Specific neuropathic pain alleviating dosage levels for antidepressants are those given in the Physicians' Desk Reference ("PDR"), 1996 Edition as well as in Goodman & Gilman's The Pharmacological Basis of Therapeutics ("Goodman & Gilman"). (Exhibits A, B)	There are several quite substantive differences in the teachings/claims of the Caruso patent and 10/772,809 which would not lead those of skill to combine with Crawford. 1. Caruso specifies in its teaching and claims that the antidepressant present in its therapeutic composition must be in an "amount sufficient to alleviate neuropathic pain" and further specifies those dosages are provided in the PDR, 1996 and Goodman & Gilman. Exhibits A & B provide these dosing specifications from these sources. As one can see, the dosage levels specified by the PDR and Goodman & Gilman are ranges 75-300 mg daily. 10/772,809 specifically calls for a low dose of a tricyclic antidepressant and defines that to be (and claims it to be) a dosage of ≤25 mg daily. 2. Caruso specifies a combination of an antidepressant and a NMDA receptor antagonist is necessarily present in the therapeutic composition. Caruso teaches that a large number of other active additional components (including acetaminophen) can be added to the composition. Consequently, the therapeutic composition of Caruso could never be

Publication	Comments	Relationship to U.S. Patent Application No. 10/772,809
		constituted by just a tricyclic antidepressant and a non-narcotic analgesic.
Matheson	Matheson does not substitute for deficiencies in Crawford with Caruso. Matheson only described rofecoxib. Matheson and Figgitt is simply a review of Rafecoxib, a (COX)-2 inhibitor.	It really stretches the imagination to postulate how those of skill would combine this publication with Crawford, and in doing so come up with the claimed invention. A determination of obviousness requires that "the scope and content of the prior art are to be determined; differences between the prior art and the claims at issue are to be ascertained; and the level of ordinary skill in the pertinent art resolved." KSR International Co. v. Teleflex, Inc., -- U.S. --, 127 S.Ct. 1727, 1734, 82 U.S.P.Q.2d 1385 (2007) quoting Graham v. John Deer Co., 383 U.S. 1, 17 (1966). "In making a determination of obviousness by looking at the teachings of multiple patents, one should consider the effects of demands known to the design community or present in the market place; and the background knowledge possessed by a person having ordinary skill in the art, all in order to determine whether there was an apparent reason to combine the known elements in the fashion claimed by the patent at issue. To facilitate review, this analysis should be made explicit."

III. The Inventor's Comments

The inventor requests that the following statement be entered in the record:

We have repeatedly made the same convincing (I believe) responses to the same rejections by the Office over a six (6) year period. Over this time course, we have had three interviews with the Office: 1. January 2007 with Examiner Abigail Cotton, 2. October 2007 with Examiner Renee Claytor and her Supervisor Sheeni Padmanabhan, and 3. July 2008 with Examiner Claytor and her Supervisor Sheeni Padmanabhan. IP Counsel from Barnes and Thornburg accompanied me to Washington for personal interviews with the Office for Interviews 1 and 2 above. Interview 3 was conducted at the Office with me on the phone. Concluding each of these interviews,

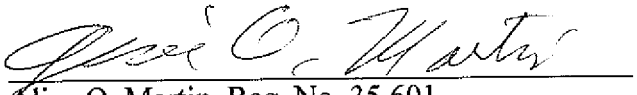
there was mutual agreement that the submission of a specific amendment should overcome the rejections. However, a long time after submission of each of the Amendments, we received the same rejections on the same basis as before, and Examiner Claytor never even entered our amendment submitted November 3, 2009.

I think it is outrageous for a very small pharmaceutical company to have had to go through the kind of unnecessary expense, prolonged delays, and disingenuous responses from the Office.

I am providing the attached Table which summarizes the profound differences between the teachings and claims of my patent applications and those of the art cited in our final rejection. This table clearly demonstrates that there is nothing anticipatory to my application contained in the cited art. I trust that a careful review of our Appeal Brief as well as the following Table will result in approval and issuance of this patent.

Allowance of claims on appeal is requested.

Respectfully submitted,



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